Heart Autonomic Function in Overweight Adolescents

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We compared factors associated with sympathetic cardiac activity in 70 male adolescents (34 obese and 36 with appropiate weight). In fasting we measured insulin, leptin, glucose, blood pressure, and heart rate variability by power spectral analysis. Obese adolescents had higher values for systolic blood pressure, insulin, leptin, low frequency/high frequency index (LF/HF) ; and lower for standard deviation of all the normal RR intervals, and total power. In the multiple regression analysis, factors associated with LF/HF index were leptin and systolic blood pressure ($R^2 = 0.18$; $P = 0.004$ for the model). We concluded that higher sympathetic activity in obese adolescents is related to higher leptin and systolic blood pressure levels.

Key words: *Adolescent, Heart, Leptin, Obesity, Overweight.*

IN a recent study in adolescents in 13 European countries, Israel, and the United States; the highest prevalence of overweight was found in the United States and the lowest in Lithuania(1). The prevalence of adolescent obesity in Mexico is reported to be 24%(2).

Overweight adolescents are more likely than lean adolescents to have hypertension in adulthood(3). Although the association between obesity and cardiovascular function is strong, the mechanism underlying this relationship is not well understood. Sympathetic nervous system is the main regulatory mechanism of cardiovascular system and it is a strong candidate to explain this association. In obese adults, plasma norepinephrine concentrations and spillover rate from sympathetic nerve terminals are greater than in lean subjects(4,5). Although cardiac sympathetic activity has been studied in adolescents(6,7), the relationship between this and various clinical traits has not been evaluated. We conducted this study to compare the cardiac sympathetic activity between obese and appropriate weight adolescents as well as to determine the relationship between heart rate variability (HRV) with anthropometric variables, blood pressure, glucose, insulin, and leptin levels.

Subjects and Methods

We studied 70 male subjects aged 12 to 17 years, with steady body weight for the last three months. All subjects had blood pressure lower than the 95th percentile according to the Task Force on Hypertension Control in Children and Adolescents(8). They were non smokers, and did not have any thyroid dysfunction, or other chronic-degenerative illnesses. None of them had received anorexigenic drugs, beta blockers agents, calcium antagonists or vasodilator drugs.

All subjects and at least one parent were informed about the purpose of the study and gave their informed consent to participate. The protocol of the study was approved by the local ethical committee.

We considered BMI-for age $\geq$95th percentile to identify obese adolescents, and >5th but <85th percentile for "appropriate weight"(9). Those adolescents with BMI between 85th to 94th percentile were not included.

As part of the demographic information we collected age, and self-report of Tanner's stage from the subjects by showing pictures of the stages of adolescent development for pubic hair distribution. Weight and standing height were obtained to calculate the body mass index (BMI), and girth values were measured to obtain the waist to hip ratio (WHR). Blood pressure levels were obtained using a mercury sphygmomanometer with a cuff covering two thirds of the right arm. Each volunteer was maintained in recumbent position for at least 15 minutes. Thereafter two readings were made within a 5 minutes interval, and the average was registered. A morning fasting blood sample was obtained to measure glucose, leptin, and insulin levels. Insulin resistance was estimated by means of the homeostatic model assessment for insulin resistance index (HOMA-IR) with the following formula: fasting serum insulin (μU/mL) × fasting plasma glucose (mmol/L) / 22.5(10).

Since the 1970s, measures of cardiovascular autonomic function have been used to evaluate clinical status in adults risk for myocardial morbidity and mortality(11). Common methods for evaluating the beat-to-beat variation in cycle length (*i.e.*, R-R interval) of each heart period include Holter monitoring for determining heart rate variability (HRV). Holter monitoring is used not only to compute the measurement of standard deviations of heart periods on the basis of sinus R-R intervals over time, but also to quantify and discriminate between sympathetic and parasympathetic autonomic function by recording the frequency (Hz) of R-R variation, also referred to as power spectral analysis(12). The sympathetic activity was evaluated with 60 minutes electrocardiograph monitoring at rest in recumbent position, from 8:00 to 10:00 h using a 3-channel Holter recorder (model GBI-3S, Galix Biomedical Instrumentation INC). The tapes were analyzed in a Holter Galix software, to obtain the heart rate variability as the SD of all the normal RR intervals (SDNN). Spectral analysis was carried out with a direct fast Fourier transform providing the spectrum of frequencies (Hz) during the recording period, and indicating the relative amount of total (0.01-1.00 Hz), low (0.04-0.15 Hz), and high (from 0.15-0.40 Hz) frequency power. We obtained the LF/HF index as a direct measured of sympathetic acivity(12). Ectopic beats were identified and excluded from analysis.

Serum insulin was measured with a solid phase radioimmunoassay (Diagnostic Products Corporation, Los Angeles, CA). The intra- and interassay coefficients of variation were 3.0 % and 4.5 %, respectively. Serum leptin was measured with an immunoradiometric assay (IRMA) (Diagnostics Systems Laboratories, Inc., Webster, Texas). The intra and interassay coefficients of variation were 3.4% and 6.7%, respectively.

Descriptive statistic is reported as means $\pm$ SD. A P value <0.05 was considered significant. Fitness to the normal distribution was carried out with the Kolmogorov-Smirnov test. Differences between obese and lean adolescents were tested with the unpaired Student's t test or the Mann-Whitney U when data showed significant departure from normality. Interaction with diverse covariates was studied by mean of a multiple linear stepwise regression analysis with forward inclusion of variables. LF/HF index was taken as the dependent variable, and BMI, WHR, blood pressure levels, insulin, and leptin as candidate regressors. For analysis the frequency domain measures of HRV were log-transformed considering their significant departure from normality. All data were analyzed using the STATISTICS software version 6.0 (Statsoft Inc. Tulsa OK).

Results

Seventy male adolescents were included in the study (34 obese and 36 with appropriate weight). The characteristics of both groups are shown in *Table I*. There was no difference on age and Tanner's stage. Obese adolescents showed higher blood pressure, LF/HF index, glucose, insulin, insulin resistance, and leptin levels. In contrast, SDNN and TP were lower in obese than in appropriate weight adolescents. Simple correlation for LF/HF index are shown in *Table II*. In the multiple regression analysis, the factors associated with LF/HF index were leptin (R = 0.33; P = 0.005), and systolic blood pressure levels (R= 0.28; P = 0.01); R^2 = 0.18; P = 0.004 for the model.

Discussion

In this study we confirmed that obese adolescents have higher blood pressure, insulin levels, and lower insulin sensitivity than lean adolescents. All of these parameters integrate the insulin resistance syndrome(13). Excess body fat, especially visceral fat, mobilizes free fatty acids in the portal circulation, which in turn reduces hepatic clearance of insulin, causing peripheral hyperinsulinemia(14).

TABLE I–*Characteristics of Study Subjects.*

Variable	Obese(n = 34) Mean ± SD	Appropriate weight (n = 36) Mean ± SD	P
Age (yr)	14.0 ± 1.1	14.3 ± 1.4	NS
Tanner's stage	3.3 ± 1.0	3.3 ± 0.7	NS
BMI	30.7 ± 3.2	20.4 ± 3.2	<0.0001
WHR	0.95 ± 0.05	0.85 ± 0.04	<0.0001
SBP (mmHg)	117 ± 8.8	107 ± 9.3	0.0001
DBP (mmHg)	74.3 ± 6.8	69.8 ± 6.4	0.006
Glucose (mmol/L)	5.0 ± 0.3	4.5 ± 0.5	0.0002
Insulin (pmol/L)	98.4 ± 93.0	33.0 ± 20.4	<0.0001
HOMA-IR	3.7 ± 2.6	1.1 ± 0.7	<0.0001
Leptin (ng/mL)	39.6 ± 15.9	9.8 ± 9.0	<0.0001
TP (ms^2)	5719 ± 2190	7488 ± 2747	0.03
SDNN (ms)	92.7 ± 24.0	106.3 ± 21.1	0.009
LF/HF	3.4 ± 1.6	2.3 ± 1.0	0.001

BMI - body mass index; DBP - diastolic blood pressure; HOMA- IR, insulin resistance index; LF/H - F low frequency to high frequency ratio; SBP- systolic blood pressure; SDNN- standard deviation of all the normal RR - intervals; TP - total power, and WHR - waist to hip ratio.

Key Messages

- Obese adolescents show heart sympathetic overactivity.
- There is relationship between heart sympathetic overactivity and systolic blood pressure levels in obese adolescents.

We found an autonomic imbalance in overweight adolescents, characterized by decrease in SDNN and total power, and increase in LF/HF index. These results are in accordance with the study of Riva, *et al*.(6) in Italian adolescents, and express imbalanced heart sympathetic activity. However, they did not consider tabaquism or menstrual cycle in female subjects, variables that modify heart sympathetic activity. This heart sympathetic overactivity is considered a mechanism for the generation of ventricular arrhythmias and sudden death(15). Although all adolescents were normotensive, blood pressure levels were higher in over-weight subjects. These blood pressure levels plus imbalanced heart sympathetic activity may predispose for cardiac complications.

Leptin levels were higher in overweight adolescents, and this was in accordance with BMI and WHR. This can be explained because adipose tissue is the main source of leptin production.

In the univariate analysis, fat tissue expressed as WHR, BMI and leptin levels as well as systolic blood pressure were associated with LF/HF index. In accordance with our results, some studies have suggested a possible relationship between leptin, sympathetic activity and hypertension(16,17). Moreover, after multiple regression it was shown that higher sympathetic activity found in obese adolescents is related to higher leptin and systolic blood pressure levels. Leptin shows a variety of effects in the hypothalamus: It reduces appetite and induces weight loss and thermogenesis(18). Leptin has also peripheral sites of action: it stimulates vascular smooth muscle proliferation and migration(19). In rats, leptin infusion increases sympathetic activity in kidneys, adrenals, and brown adipose tissue. As a result, vascular resistance and blood pressure are increased (20). Thus, higher systolic blood pressure observed in overweight subjects, and the association between this variable with LF/HF index could be the result of the imbalanced heart sympathetic activity and leptin levels.

TABLE II–*Simple Correlation for LF/HF Index.*

Variable	R	P
Body mass index	0.32	0.005
Waist hip ratio	0.30	0.009
Leptin	0.30	0.007
Systolic blood pressure (mmHg)	0.33	0.001

A limitation of our study was the lack of female adolescents, however there are gender differences in many hormonal levels that make it difficult to compare them together.

It is important to design long term studies in overweight adolescents to know the relationship between these metabolic disorders and imbalanced heart sympathetic activity with cardiovascular diseases as well as potential treatment.

In conclusion, overweight male adolescents of a developing nation have imbalanced heart sympathetic activity, and higher blood pressure levels than appropriate weight adolescents that may predispose them to cardiac complications. Imbalanced heart sympathetic activity was associated with leptin and systolic blood pressure levels.

Contributors: GJM concept and design, interpretation of data, revising the article critically, and final approval; AR, SG and RG: acquisition of data, analysis and interpretetion of data. AN Concept and design, interpretation of data, acquisition of data and revising the article critically.

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Effect of Enteral and Parenteral Nutrition on Growth Parameters of Hospitalized Turkish Children

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This study was conducted to investigate growth and the complications in the hospitalized pediatric patients receiving either enteral (n = 26) or parenteral (n = 15) nutrition. Anthropometric measures as well as the results of biochemical analyses and complete blood counts were recorded. Weight, height and weight for height were expressed in z scores. The improvement in z scores for the 26 children receiving enteral nutrition in weight for age (P = 0.001), height for age (P = 0.002) and weight for height (P = 0.008) were all statistically significant. There were also significant correlations between the changes in weight for age (r^2 = 0.15, P = 0.0049) and height for age (r^2 = 0.64 and P = 0.0001) z scores and the time for follow up. Corresponding z scores in the parenteral nutrition group were not statistically significant. This study indicated that enteral nutrition provides significant improvement not only in weight but also height of sick hospitalized pediatric patients.

Key words: *Enteral, Growth, Nutrition, Parenteral.*

WITH the recognition of the untoward effects of malnutrition in hospitalized pediatric patients, enteral and parenteral nutrition have gained attention especially for the critical and chronically ill patients(1,2). The number of patients receiving enteral and parenteral nutrition in the hospital or even at home is increasing everyday(3-5). The accelerated progression in pediatric enteral and parenteral nutrition has led to the development of new nutrition techniques such as percutaneous endoscopic gastrostomy(6).

For about two years, severely, moderately or chronically ill patients in the pediatric ward of Gazi University Hospital, have been nutritionally supported by the nutrition team of Department of Pediatric Metabolism and Nutrition. In this retrospective study, the